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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/818,990	03/27/2001	D. Wade Walke	LEX-0152-USA	9270

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EXAMINER	
SWOPE, SHERIDAN	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 05/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/818,990	WALKE ET AL.	
	Examiner	Art Unit	
	Sheridan L. Swope	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 6-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 6-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-3 and 6-10 are pending.

In view of the telephonic Interview with David Hibler on April 30, 2004, PROSECUTION IS HEREBY REOPENED. A new ground of rejection is set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

Claim Rejections - 35 USC § 101

Claims 1-3 and 6-10 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Claims 1-3 and 6-10 are directed to isolated polynucleotides encoding a novel protein. The specification discloses that the claimed polynucleotides encode "proteins that share sequence similarity with mammalian membrane and structural proteins" (pg 1, lines 9-10). The specification further states that "The novel human proteins described... share structural similarity with *inter alia*, mammalian muscle proteins (myosin light chain kinase, telokin, IgG like C2 domains, motilin), and modifiers and anchors of thereof (pg 2, lines 1-5). The specification asserts that "The novel human nucleic acid sequences described herein, encode

alternative proteins/open reading frames of 1,320, 376, 419, 401, 459, 570, 754, 1,045, 102, 144, 126, 184, 295, and 479 amino acids in length (myosin light chain/titin-like protein), SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, and 28 respectively" (pg 2, lines 6-11).

While the specification states that the claimed polynucleotides encode proteins having structural similarity with mammalian membrane and structural proteins as well as mammalian muscle proteins (myosin light chain kinase, telokin, IgG like C2 domains, motilin), and modifiers and anchors of thereof, this disclosure of structural similarity is not an assertion of function or utility. The specification contains NO assertion of the function(s) present in the claimed polynucleotide or the proteins encoded thereby. Furthermore, while the specification asserts that the claimed polynucleotides encode alternative proteins/open reading frames of various lengths (myosin light chain/titin-like proteins), the claimed invention does not meet the utility requirements for the following reasons.

Even assuming arguendo that the specification asserts that the claimed polynucleotides encode a polypeptide having myosin light chain (pg 2, line 9), myosin light chain kinase (pg 2, line 2), or titin activity, which assertion is not present, here is no experimental evidence to support the assertion that the claimed polynucleotides encode a polypeptide having the function of myosin light chain, myosin light chain kinase, or titin. The alleged asserted function for the claimed polynucleotides has been determined solely on the basis of structural similarity (i.e. sequence homology). The state of the art clearly teaches the unpredictability of assigning function based on sequence homology and acknowledges that, small changes can drastically change function. Bork et al, 2000, Smith et al, 1997 and Brenner, 1999 are some of the references that describe the overall state of the art in regard to the unpredictability of annotating

function. Bork et al teaches the pitfalls associated with comparative sequence analysis for predicting protein function because of known error margins for high-throughput computational methods. Bork et al also indicates that one of the causes of this inaccuracy is that the quality of data available is still insufficient, especially data relating to protein function. Furthermore, Bork et al teaches that protein function is context dependent, and both molecular and cellular aspects must be considered (pg 398). Smith et al. indicates that there are numerous cases in which proteins of very different functions are homologous (pg 1222, third col, last parg). In addition, Brenner teaches the difficulty of accurately inferring function from homology and clearly states that most homologs must have different molecular and cellular functions (pg 132, col 2, parg 2). Examples, of pitfalls associated with comparative sequence analysis for predicting function, are shown by Broun et al, 1998 and Van de Loo et al, 1995. Van de Loo et al. teaches that polypeptides of approximately 67% homology to a desaturase from *Arabidopsis* where found to be hydroxylases, once tested for activity. Broun et al. teaches that as few as four amino acid substitutions can convert an oleate 12-desaturase into a hydrolase and as few as six amino acid substitutions can transform a hydrolase to a desaturase.

At the time of filing of the instant application, the sequence having highest homology with SEQ ID NO: 1 was the polynucleotide of Hillier et al, 1996 (Genbank Acc# AA179499), which has 100% identity with residues 68-337. The function of the polynucleotide of Hillier, and the polypeptide encoded thereby, is not known. However, the polynucleotide of Hillier has 98% identity with a polynucleotide taught by Zheng et al, 1990, which encodes the BTF3b transcription factor. Homology of SEQ ID NO: 1 with the polynucleotides of Hillier et al and Zheng et al teaches away from Appellant's presumed assertion that SEQ ID NO: 1 encodes a

myosin light chain, a myosin light chain kinase, or a titin-like protein. Furthermore, SEQ ID NO: 2 has no detectable homology with myosin light chain or myosin light chain kinase and only 11.6% identity with human cardiac titin (Musco et al 1995). In view of the unpredictability of annotating function based on sequence homology as well as the low sequence homology between the polynucleotides/polypeptide of the instant application and polynucleotides/polypeptides having myosin light chain, myosin light chain kinase, or titin-like function as well as the homology of the instant polynucleotide to a polynucleotide encoding a protein with wholly different function (Zeng et al), one of skill in the art cannot reasonably conclude that the asserted function for the polypeptide encoded by the claimed polynucleotides is that of myosin light chain, myosin light chain kinase, or a titin-like structural protein without additional supporting evidence such as, an indication of which are the critical structural elements present in the claimed polynucleotides that are characteristic of other polynucleotides encoding myosin light chain, myosin light chain kinase, or titin, or experimental evidence of the claimed function. In the instant case, the specification fails to provide any information or experimental evidence that would support Appellant's alleged asserted biological function.

In addition, even if one assumes that the asserted function for the polypeptide encoded by the claimed polynucleotides is that of myosin light chain, myosin light chain kinase, or a titin-like protein, the specification fails to disclose sufficient information to conclude that there is a substantial and specific utility associated with the "myosin light chain, myosin light chain kinase, or a titin-like" polynucleotide/polypeptide of the instant invention. The specification discloses that, in general, proteins are known to provide structural and mechanical scaffolding, serve as recognition markers, mediate signal transduction, and mediate translocation of molecules

through the lipid bilayer (pg 1, parg 2). The specification further discloses that functional equivalents for the polypeptide of SEQ ID NO: 2 would have "the ability to bind and cleave a substrate of NHP [said polypeptide], or the ability to effect an identical or complementary downstream pathway, or a change in cellular metabolism (e.g., proteolytic activity, ion flux, tyrosine phosphorylation etc.)". Such a diverse list of possible activities for what the function of the protein set forth by SEQ ID NO: 2 might be does not disclose what the function is, i.e. what does one use a myosin light chain, myosin light chain kinase, or titin-like protein for?

The specification also asserts that the claimed polynucleotides can be used for identification of the coding sequence and mapping of polynucleotides to a particular chromosome (page 2, lines 31-33); to screen libraries, isolate clones, and prepare cloning and sequenceing templates (pg 5, lines 29-31); in microarrays, or other assays; to screen genetic material from patients; identification of mutations associated with SEQ ID NO: 1; in hybridization assays; for analysis of expression patterns; for identification of molecular targets; and for identification of disease-related mutations (pgs 6-8); and to study protein evolution (pg 16, line 27). These utilities are not considered substantial and specific for the following reasons. The specification fails to disclose sufficient information in regard to the biological significance or further characterization of the claimed polynucleotides and the proteins encoded thereby, which would be necessary for an artisan to know how to use the claimed polynucleotides. Such as: (1) the biochemical activity of the polypeptide being encoded by the claimed polynucleotides, (2) the cellular processes or pathways in which the recited protein is involved, (3) the molecular interactions associated with the recited protein, or (4) any diseases linked to mutation/polymorphism of the recited polynucleotides and encoded proteins, such that a specific

use for the claimed polynucleotides would be apparent. If information in regard to the biological role of the claimed invention were to be presented, several utilities could be apparent for the claimed polypeptide, such as purification of regulatory factors or diagnostic identification of diseases due to mutation of said protein; however, these utilities require additional information, which is not presented by the specification. As known in the art and admitted by Appellants in the specification, proteins are active in many different biological processes (pg 1, lines 21-24). Since, the cellular function of the recited protein, the biological processes associated with said protein, and any diseases due to mutation of said protein are all unknown, the utilities recited in the specification are not substantial, as they will require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. See e.g., Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966). The instant situation is analogous to the lack of substantial utility examples provided by MPEP § 2107.01 in that basic research is required to study the properties of the claimed polynucleotides and the corresponding polypeptide as well as the mechanisms in which the claimed polynucleotides are involved. In addition, while one could argue that some of the recited uses are specific, such as being a probe to be used in microarrays or in mapping of nucleotides in a particular chromosome, it is noted that these uses are not specific due to the fact that, all other human polynucleotides can be used as probes in microarrays or in mapping of nucleotides in the chromosome and Appellants have not provided reasons why one of skill would be motivated to use the instant polynucleotides. Since the instant specification does not disclose a credible, specific and substantial "real world" use for the polynucleotide of SEQ ID NO: 1 or any polynucleotide encoding the polypeptide of

SEQ ID NO: 2, then the claimed invention, as disclosed, does not meet the requirements of 35 U.S.C. §101 as being useful.

Claim Rejections - 35 USC §112, first paragraph

Claims 1-3 and 6-10 are also rejected under 35 U.S.C. 112, first paragraph, for lack of enablement. Specifically, since the claimed invention is not supported by either a substantial and specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Even if the polynucleotides encoding SEQ ID NO: 2 were found to have a patentable utility and, thus, the Invention of Claims 1-3 and 6-10 was not rejected under 35 U.S.C. 101/112, first paragraph, for lack of utility, Claim 1 would still be rejected under 35 U.S.C. 112, first paragraph, for lack of enablement of the entire scope of the claimed invention for the following reasons. Claim 1 is so broad as to encompass any polynucleotide sequence comprising at least 2000 contiguous bases of SEQ ID NO: 1. Neither the specification nor the prior art teach a skilled artisan how to use all said polynucleotides. The specification does not support the broad scope of Claim 1 because the specification does not establish: (A) the activity of any polypeptides encoded by polynucleotide sequences comprising at least 2000 contiguous bases of SEQ ID NO: 1; (B) regions of the structure of the polypeptide encoded by SEQ ID NO: 1 which may be modified without effecting the activity of said polypeptide; (C) the general tolerance of the activity of the polypeptide encoded by SEQ ID NO: 1 to modification and extent of such tolerance; (D) a rational and predictable scheme for modifying the polypeptide encoded by SEQ ID NO: 1 with an expectation of obtaining the desired biological function; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible

choices is likely to be successful. Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of polynucleotide sequences comprising at least 2000 contiguous bases of SEQ ID NO: 1.

Claims 7 and 10, as reciting vectors and host cells comprising the nucleic acid molecules of Claim 1 are rejected under 35 U.S.C. 112, first paragraph, for lack of enablement for the same reasons.

Likewise, even if the polynucleotides encoding SEQ ID NO: 2 were found to have patentable utility, Claim 1 would also still be rejected under 35 U.S.C. 112, first paragraph, for insufficient written description of the claimed invention. Claim 1 fails to describe any activity for any protein encoded by any species of the genus of nucleic acid molecules recited and the specification does not contain any disclosure of the functions of said genus of nucleic acid sequences. SEQ ID NO: 1 consists of 3963 bases, which encode the 1320 amino acid residues of SEQ ID NO: 2. Thus, the genus of polynucleotides recited by Claim 1, comprising at least 2000 contiguous bases of SEQ ID NO: 1, has the potentiality of encoding many different peptide fragments with different functions or with no function. Therefore, many functionally unrelated polynucleotides are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only one species of the claimed genus, SEQ ID NO: 1, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Because the specification fails to disclose a function for the recited fragments of SEQ ID NO: 1, one of skill in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time of filing. Claims 7 and 10, as

reciting vectors and host cells comprising the nucleic acid molecules of Claim 1 are rejected under 35 U.S.C. 112, first paragraph, for insufficient written description for the same reasons. Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Applicants provided arguments in the Appeal Brief filed December 2, 2003 to support their request that rejection of Claims 1-3 and 6-10 under 35 U.S.C. 101/112, first paragraph, be withdrawn. Said arguments are not found to be persuasive for the reasons set forth in the Examiner's Answer mailed March 3, 2004.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Sheridan Lee Swope, Ph.D.

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